

## Safety of elective hepatectomy performed on weekend for patients with hepatocellular carcinoma

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The incidence of hepatocellular carcinoma (HCC) is increasing year by year. The International Agency for Research on Cancer (IARC) reported that more than 630,000 people were diagnosed with HCC in 2020 and more than half of new cases of HCC were in China. The increasing number of patients overburdens the medical system and the waiting time before the surgery becomes longer and longer. This poses a new challenge to the applicability of traditional surgical management model. The elective surgery performed on weekend could provide an efficient solution to the problem. However, the safety of weekend surgery is controversial because surgical patients have a higher severe complication incidence and postoperative mortality on the weekend compared to the weekday (*ie*, weekend effect). Glance *et al*<sup>[1]</sup> reported that patients in America undergoing moderate-to-high risk surgery on the weekend have a clinically significantly increased risk of death and major complications compared with a similar surgery on a weekday.

However, these studies did not provide a strong evidence for weekend hepatectomy. First, the inclusion criteria of these studies were broad, mixed with different departments and surgeries. Second, these studies only focused on perioperative complications and mortality, and the long-term prognosis was not clear. Finally, in previous studies, weekend surgeries were almost emergency surgeries. To our knowledge, routine elective surgery on Saturday or Sunday has rarely been studied. Therefore, we aim to investigate the short- and long-term prognosis of weekend hepatectomy through analyzing cases of a large study population in a high-volume center. Our results can help the clinicians to allocate medical resources and manage surgeries more effectively.

Patients who had undergone hepatectomy for HCC between May 2014 and July 2019 at the West China Hospital of Sichuan University were considered. In West China Hospital, various elective surgeries could be

routinely performed on Saturdays. The principle of voluntary was adopted; doctors could perform weekend surgery according to their personal condition and clinical needs. This study was conducted in accordance to the ethical guidelines of the 1975 *Declaration of Helsinki* and was approved by the Ethics Committee of West China Hospital, Sichuan University. The requirements for informed consent were waived because of the retrospective nature of the study.

The inclusion criteria are as follows: (1) primary hepatectomy; (2) pathologically proven to be HCC; (3) elective operation; and (4) continuous follow-up or medical records are available. The exclusion criteria are as follows: (1) incomplete clinical or operative information; (2) HCC with rupture and bleeding; (3) combined splenectomy or biliary-intestinal anastomosis; (4) complicated with extrahepatic invasion; (5) other malignancies were found after hepatectomy; and (6) positive surgical margin. The study enrolled 1646 patients who underwent elective hepatectomy after careful evaluation. Elective hepatectomy were divided into two groups based on the date of surgery: weekday and weekend groups. Propensity score matching (PSM) was adopted to overcome potential selection bias. All statistical analyses were performed using R version 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria).

All data for demographics and surgical information were obtained from Hospital Information System (HIS). Postoperative complications were measured by the Clavien-Dindo classification and Comprehensive Complication Index (CCI). The primary endpoints were overall survival (OS) and recurrence-free survival (RFS). For patients who received liver transplantation, the date of the operation was considered to trigger the endpoint event. The final follow-up was conducted on January 31, 2021.

Overall, a total of 1646 HCC patients underwent elective hepatectomy and were divided into two groups. A total of 207 patients accounting for 12.58% of the total received

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weekend hepatectomy. The weekend group had more hypertension patients (20.77% *vs.* 15.29%,  $P=0.044$ ). Notably, the higher model for end-stage liver disease (MELD) score in the weekday group indicated worse liver function in this group (6.51 [7.16, 7.97] *vs.* 6.73 [7.37, 8.24],  $P=0.014$ ). But the same conclusion was not found in comparisons of the Child-Pugh classification, albumin-bilirubin (ALBI) scoring model classification, and indocyanine green (ICG) test. It was noted that more patients in the weekend group met the Milan criteria (53.62% *vs.* 46.00%,  $P=0.040$ ). But the statistical difference was not confirmed in Barcelona Clinic Liver Cancer (BCLC) stage. Interestingly, liver surgeons preferred to perform weekend operations in the morning (61.35% *vs.* 48.78%,  $P=0.001$ ). In terms of pathological parameters, the difference between the two groups was more significant in surgical margin > 10 mm (53.00% *vs.* 39.75%,  $P=0.002$ ), multiple nodules (11.58% *vs.* 17.03%,  $P=0.048$ ), cirrhosis (59.42% *vs.* 50.24%,  $P=0.014$ ), and satellite lesions (3.86% *vs.* 9.10%,  $P=0.011$ ) [Supplementary Figure 1, <http://links.lww.com/CM9/A743>, Supplementary Table 1, <http://links.lww.com/CM9/A744>].

After 1:1 PSM, 207 patients were selected. The following variables were included to match: age, gender, antiviral agent, Hepatitis B virus (HBV)-DNA > 1000 IU/mL, hypertension, diabetes mellitus, anatomical hepatectomy, surgical margin > 10 mm, major hepatectomy, laparoscope, BCLC stage, multiple tumor, tumor diameter, differentiation grade, satellite lesions, microvascular invasion (MVI), cirrhosis, non-alcoholic fatty liver disease (NAFLD), hepatitis B surface antigen (HBsAg), hepatitis C core antibody (HCVAb), alpha fetoprotein (AFP) > 400 ng/mL, neutrophil to leukocyte ratio (NLR) and platelet to leukocyte ratio (PLR) before surgery, Child-Pugh classification, ALBI classification, MELD score, and surgical period.

In terms of short-term prognosis, after PSM, the length of stay (LOS) (1.00 [8.00, 12.00] *vs.* 10.00 [8.00, 14.00],  $P=0.170$ ) and 90-day mortality (3.38% *vs.* 5.79%  $P=0.240$ ) for patients who underwent elective hepatectomy were similar. At the same time, no statistical difference was found in both severe complications (Clavien-Dindo class  $\geq 3$ ) (4.83% *vs.* 6.82%  $P=0.520$ ) and CCI (8.70 [0.00, 8.70] *vs.* 8.70 [0.00, 12.20],  $P=0.123$ ). The weekday group had a higher rate of nausea and vomiting (2.42% *vs.* 3.86%,  $P=0.005$ ), which reflected lower patients' comfort level after the surgery indirectly. Also, the pulmonary infection was more common in the weekday group (0.00% *vs.* 1.93%,  $P=0.044$ ). The short-term outcome information are reported in Supplementary Table 2, <http://links.lww.com/CM9/A744>.

In terms of long-term prognosis, the median follow-up duration was 34.2 months. A total of 645 patients accounting for 39.19% of the total died at the last follow-up. Also, 912 patients accounting for 55.21% of the total recurred during our consecutive follow-up. Weekday group patients had better OS than weekend group ones (at 5 years: 52.66% *vs.* 61.99%,  $P=0.024$ ; Figure 1A). Meanwhile, RFS was worse in the weekday group (59.22% *vs.* 55.40%,  $P=0.240$ ; Figure 1B), but the difference was not significant. After adjusting PSM to 1:1,

no statistically significant difference was found in OS between the two groups (at 5 years: 52.66% *vs.* 57.00%,  $P=0.610$ ; Figure 1C). The similar result was also found in the comparison of RFS (at 5 years: 59.22% *vs.* 53.96%,  $P=0.450$ ; Figure 1D).

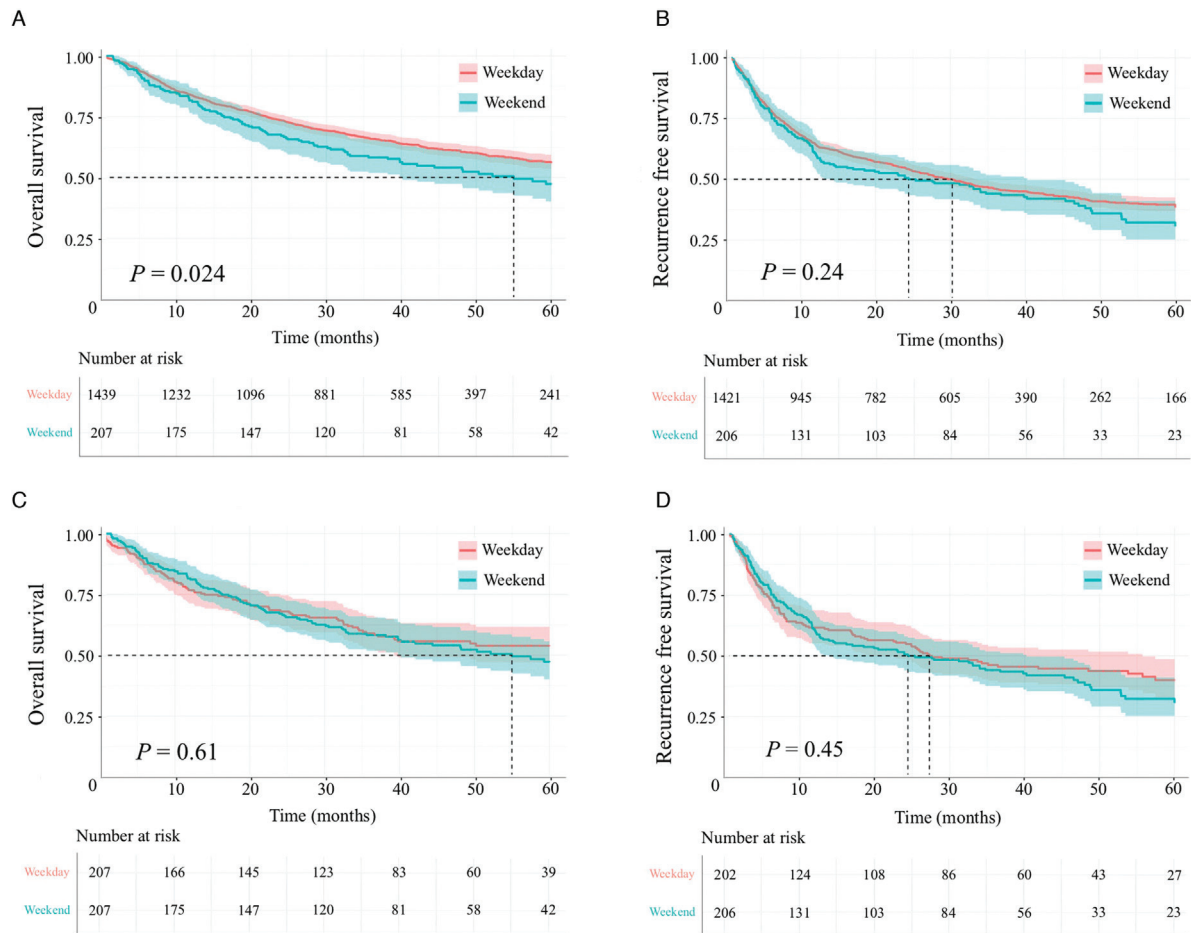
Cox regression models revealed the associated risk factors for our study population. In the multivariate, the presence of weekend hepatectomy had no impact on prognosis [Supplementary Table 3, <http://links.lww.com/CM9/A744>].

The above results show that the hepatectomy for HCC performed on weekends is safe. After matching patients in weekday group with weekend group by propensity score at 1:1, no statistical difference was found in short- and long-term prognosis. Some previous studies have reported that patients undergoing surgery could experience higher mortality and worse outcomes. However, the objects of these studies are emergency surgery, the elective hepatectomy has not been discussed.<sup>[2-4]</sup> Besides, the evaluation of long-term outcomes was lacking in these studies.<sup>[5-7]</sup> From the perspective of our study population, patients in weekend group had a worse liver function, higher incidence of cirrhosis, and lower rate of in taking antiviral drugs. It could be the reason why patients in weekend group had a worse OS before PSM. Liver surgeons selected more patients with single tumor and meeting Milan criteria which could indicate that surgeons were more inclined to perform low-difficulty surgery on the weekend. The lesser tumor burden led to a wider surgical margin. Furthermore, more satellite lesions in weekday group and more lymphatic invasion in weekend group also showed the existence of the heterogeneity. It provided the applicable premise to conduct PSM. After PSM, the prognosis of the two groups was similar. Practical experience of 5 years showed that the weekend effect did not affect the elective hepatectomy performed on weekends.

To ensure the perioperative safety of surgical patients, West China hospital adopted various effective measures. To protect patients' safety, the number of staff working on weekends was the same as on weekdays in the hospital. Therefore, various laboratory and imaging examinations and medical interventions could be carried out routinely on weekend, which improved the quality of medical care provided on weekends. Besides, the patients performing the hepatectomy for HCC on weekend received more careful preoperative evaluation. Therefore, both doctors and patients can be benefited.

The rights and interests of doctors and patients were also protected. Flexible work and rest management system limited doctors' working hours and provided more freedom in scheduling. At the same time, the shorter waiting time for admission and the same medical costs make the weekend hepatectomy obtain a wide range of support from HCC patients. Under the dual premise of government support and reasonable system, the weekend surgery is a win-win for both the surgeons and the patients.

In summary, our study suggested that weekend hepatectomy for HCC was safe. Our study provided a strong evidence to clarify the safety and rationality of weekend



**Figure 1:** OS and RFS durations before and after PSM in the weekday and weekend groups. (A) OS before PSM ( $P = 0.024$ ). (B) RFS before PSM ( $P = 0.240$ ). The RFS analysis included 1627 patients, and patients with an unknown recurrence status ( $n = 19$ ) were excluded. (C) OS after PSM ( $P = 0.610$ ). (D) RFS after PSM ( $P = 0.450$ ). The RFS analysis included 408 patients, and patients with an unknown recurrence status ( $n = 6$ ) were excluded. OS: Overall survival; PSM: Propensity score matching; RFS: Recurrence-free survival.

hepatectomy. We believe that under the impact of the epidemic of COVID-19, the aging population and the increasing incidence of cancer, more patients can benefit from the elective weekend surgery.

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**Conflicts of interest**

None.

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